

INFORMATION DISCLOSURE STATEMENT

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants direct the Examiner's attention to the following references which are listed on the PTO-1449 form attached hereto as **Exhibit A**. Copies of references 1-7, 9-10, 13, 16, 18, 20, 27-30, 33, 36-37, 40, 43, 45-50, 55-56, 58, 60, 63-69, 73, 78, 82, 87, 90-99, 105, 109, 111-112 and 114 are attached hereto as **Exhibits 1-58** respectively.

1. U.S. Patent No. 6,387,656 B1, issued May 14, 2002 to Jessell et al. (**Exhibit 1**);
2. PCT International Application No. PCT/US99/22517, filed September 29, 1999, International Publication No. WO00/18884, published April 6, 2000 on behalf of The Trustees of Columbia University in the City of New York (**Exhibit 2**);
3. U.S. Serial No. 10/095,932, filed March 11, 2002 on behalf of Thomas M. Jessell et al. (**Exhibit 3**);
4. Ahlgren, U. et al. (1996) "The Morphogenesis of the Pancreatic Mesenchyme Is Uncoupled from That of the Pancreatic Epithelium in IPF1/PDX1-deficient Mice", *Development* 122:1409-1416 (**Exhibit 4**);
5. Ahlgren, U. et al. (1997) "Independent Requirement for ISL1 in Formation of Pancreatic Mesenchyme and Islet Cells", *Nature* 385:257-260 (**Exhibit 5**);

6. Ahlgren, U. et al. (1998) " β -Cell-Specific Inactivation of the Mouse *Ipfl/Pdx1* Gene Results in Loss Of the β -Cell Phenotype And Maturity Onset Diabetes", *Genes & Dev.* 12:1763-1768 (**Exhibit 6**);
7. Aigner, L., et al. (1995) "Overexpression of the Neural Growth-Associated Protein GAP-43 Induces Nerve Sprouting in the Adult Nervous System of Transgenic Mice", *Cell* 83:269-278 (**Exhibit 7**);
8. Anderson, D.J. et al. (1997) "The Determination of the Neuronal Phenotype" in *MOLECULAR AND CELLULAR APPROACHES TO NEURAL DEVELOPMENT*, eds. Cowan, W.M., Jessell, T.M., and Zipursky, S.L. (Oxford University Press; New York, Oxford), pp. 26-63;
9. Apelqvist, Å., et al. (1997) "Sonic Hedgehog Directs Specialised Mesoderm Differentiation in the Intestine and Pancreas", *Current Biology* 7:801-804 (**Exhibit 8**);
10. Appel, B., (1999) "LIMitless Combinations?", *Neuron* 22:3-5 (**Exhibit 9**);
11. Arber et al. (1999) "Requirement for the Homeobox Gene *Hb9* in the Consolidation of Motor Neuron Identity", *Neuron* 23:659-674;
12. Bang, A.G. et al. (1996) "Regulation of Vertebrate Neural Cell Fate by Transcription Factors", *Curr. Opin.*

Neurobiol. 6:25-32;

13. Barber, R.P. et al. (1991) Generation Patterns of Immunocytochemically Identified Cholinergic Neurons at Autonomic Levels of the Rat Spinal Cord. *J. Comp. Neurol.* 311:509-519 (**Exhibit 10**);
14. Basler, K. et al. (1993) "Control of Cell Pattern in the Neural Tube: Regulation of Cell Differentiation by Dorsalin-1, a Novel TGF Beta Family Member", *Cell* 73:687-702;
15. Begley, C.G. et al. (1992) "Molecular Characterization of *nscl*, a Gene Encoding a Helix-loop-helix Protein Expressed in the Developing Nervous System", *Proc. Natl. Acad. Sci. USA* 89:38-42;
16. Bitgood, M.J. et al. (1995) "*Hedgehog* and *Bmp* Genes Are Coexpressed at Many Diverse Sites of Cell-Cell Interaction in the Mouse Embryo", *Dev. Biol.* 172:126-138 (**Exhibit 11**);
17. Branch, A.D. (1998) "A Good Antisense Molecule Is Hard To Find", *Trends in Biochemical Sciences* 23: 45-50;
18. Briscoe, J. et al. (1999) "Homeobox Gene *Nkx2.2* and Specification of Neuronal Identity by Graded Sonic hedgehog Signalling", *Nature* 398:622-627 (**Exhibit 12**);
19. Burke, A.C. et al. (1996) "Virally Mediated Misexpression

of *Hoxc-6* in the Cervical Mesoderm Results in Spinal Nerve Truncations", *Dev. Biol.* 178:192-197;

20. Cepko, C.L. (1999) "The Roles of Intrinsic and Extrinsic Cues and bHLH Genes in the Determination of Retinal Cell Fates", *Curr. Opin. Neurobiol* 9:37-46 (**Exhibit 13**);
21. Chen, R. et al. (1997) "Dachshund and Eyes Absent Proteins Form a Complex and Function Synergistically to Induce Ectopic Eye Development in *Drosophila*", *Cell* 91:893-903;
22. Chiang, C. et al. (1996) "Cyclopia and Defective Axial Patterning in Mice Lacking Sonic Hedgehog Gene Function", *Nature* 383:407-413;
23. Crook, ed. (1998) in *BASIC PRINCIPLES OF ANTISENSE THERAPEUTICS* (Springer-Verlag; New York), pp. 1 and 4;
24. Database Tumor Gene Index (June 1998) Accession No. A1560820. NCI-CGAP. National Cancer Institute, Cancer Genome Anatomy Project (CGAP), Tumor Gene Index;
25. Deguchi et al. (1991) "Nucleotide Sequence of a Novel Diverged Human Homeobox Gene Encodes a DNA Binding Protein", *Nucleic Acids Research* 19:3742;
26. Ding, Q. et al. (1998) "Diminished Sonic Hedgehog Signaling and Lack of Floor Plate Differentiation in *Gli2* Mutant Mice", *Development* 125:2533-2543;

27. Dutta, S. et al. (1998) "Regulatory Factor Linked to Late-Onset Diabetes?", *Nature* 392:560 (**Exhibit 14**);
28. Edlund, H. (1998) "Perspectives in Diabetes: Transcribing Pancreas", *Diabetes* 47:1817-1823 (**Exhibit 15**);
29. Edlund, T. et al. (1999) "Progression from Extrinsic to Intrinsic Signaling in Cell Fate Specification: a View from the Nervous System", *Cell* 96:211-224 (**Exhibit 16**);
30. Ensini, M. et al. (1998) "The Control of Rostrocaudal Pattern in the Developing Spinal Cord: Specification of Motor Neuron Subtype Identity Is Initiated by Signals from Paraxial Mesoderm", *Development* 125:969-982 (**Exhibit 17**);
31. Ericson, J. et al. (1992) "Early Stages of Motor Neuron Differentiation Revealed by Expression of Homeobox Gene *Islet-1*", *Science* 256:1555-60;
32. Ericson, J. et al. (1996) "Two Critical Periods of Sonic Hedgehog Signaling Required for the Specification of Motor Neuron Identity", *Cell* 87:661-673;
33. Ericson, J. et al. (1997) "Graded Sonic Hedgehog Signaling and the Specification of Cell Fate in the Ventral Neural Tube", *Cold Spring Harbor Symp. Quant. Biol.* 62:451-466 (**Exhibit 18**);

Applicants: Thomas M. Jessell, et al.
U.S. Serial No: 09/820,598
Filed: March 29, 2001
Page 24

34. Ericson, J. et al. (1997) "Pax6 Controls Progenitor Cell Identity and Neuronal Fate in Response to Graded Shh Signaling", *Cell* 90:169-180;
35. Fedtsova, N. et al. (1997) "Inhibitory Effects of Ventral Signals on the Development of Brn-3.0-expressing Neurons in the Dorsal Spinal Cord", *Dev. Biol.* 190:18-31;
36. Goridis, C. (1999) "Transcriptional Control of Neurotransmitter Phenotype", *Curr. Opin. Neurobiol.* 9:47-53 (**Exhibit 19**);
37. Goulding, M. (1998) "Specifying Motor Neurons and Their Connections", *Neuron* 21:943-946 (**Exhibit 20**);
38. Halder, G. et al. (1995) "Induction of Ectopic Eyes by Targeted Expression of the Eyeless Gene in Drosophila", *Science* 267:1788-1792;
39. Harrison, K.A. et al. (1994) "A Novel Human Homeobox Gene Distantly Related to Proboscipedia Is Expressed in Lymphoid and Pancreatic Tissues", *J. Biol. Chem.* 269:19968-19975;
40. Hebrok, M. et al. (1998) "Notochord Repression of Endodermal Sonic Hedgehog Permits Pancreas Development", *Genes & Dev.* 12:1705-1713 (**Exhibit 21**);
41. Hynes, M. et al. (1997) "Control of Cell Pattern in the Neural Tube by the Zinc Finger Transcription Factor and

Oncogene Gli-1", *Neuron* 19:15-26;

42. Ingham, P.W. (1995) "Signaling by Hedgehog Family Proteins in *Drosophila* and Vertebrate Development", *Curr. Opin. Genet. Dev.* 5:492-498;
43. Jonsson, J. et al. (1994) "Insulin-Promoter-Factor 1 is Required for Pancreas Development in Mice", *Nature* 371:606-609 (**Exhibit 22**);
44. Jurata, L.W. et al. (1998) "The Nuclear LIM Domain Interactor Nli Mediates Homo-and Heterodimerization of Lim Domain Transcription Factors", *J. Biol. Chem.* 273:3152-3157;
45. Kalter, H. (1993) "Case Reports of Malformations Associated with Maternal Diabetes: History and Critique", *Clin. Genet.* 43:174-179 (**Exhibit 23**);
46. Kim, S.K. et al. (1997) "Notochord to Endoderm Signaling is Required for Pancreas Development", *Development* 124:4243-4252 (**Exhibit 24**);
47. Krapp, A. et al. (1998) "The bHLH Protein PTF1-p48 is Essential for the Formation of the Exocrine and the Correct Spatial Organization of the Endocrine Pancreas", *Genes & Dev.* 12:3752-3763 (**Exhibit 25**);
48. Lance-Jones, C. et al. (1981) "Pathway Selection by Embryonic Chick Motoneurons in an Experimentally Altered

Environment", Proceedings of the Royal Society of London, Series B, Biological Sciences 214:19-52 (Exhibit 26);

49. Landmesser, L. (1978a) "The Distribution of Motorneurons Supplying Chick Hind Limb Muscles", *J. Physiol.* 284:371-389 (Exhibit 27);
50. Landmesser, L. (1978b) "The Development of Motor Projection Patterns in the Chick Hind Limb", *J. Physiol.* 284:391-414 (Exhibit 28);
51. Langman, J. et al. (1966) "Behavior of Neuroepithelial Cells During Closure of the Neural Tube", *J. Comp. Neurol.* 127:399-411;
52. Leber, S.M. et al. (1995) "Migratory Paths of Neurons and Glia in the Embryonic Chick Spinal Cord", *J. Neurosci.* 15:1236-1248;
53. Lee, J. et al. (1997) "Gli1 Is a Target of Sonic Hedgehog That Induces Ventral Neural Tube Development", *Development* 124:2537-2552;
54. Liem, K.F. et al. (1997) "A Role for the Roof Plate and its Resident TGF-beta-related Proteins in Neuronal Patterning in the Dorsal Spinal Cord", *Cell* 91:127-138;
55. Lin, J.H. et al. (1998) "Functionally Related Motor Neuron Pool and Muscle Sensory Afferent Subtypes Defined by Coordinate *ETS* Gene Expression", *Cell* 95:393-407

(Exhibit 29);

56. Liu, I.S.C. et al. (1994) "Developmental Expression of a Novel Murine Homeobox Gene (*Chx10*): Evidence for Roles in Determination of the Neuroretina and Inner Nuclear Layer", *Neuron* 13:377-393 (Exhibit 30);
57. Lo, L. et al. (1998) "MASH1 Activates Expression of the Paired Homeodomain Transcription Factor *Phox2a*, and Couples Pan-neuronal and Subtype-specific Components of Autonomic Neuronal Identity", *Development* 125:609-620;
58. Lo, L. et al. (1999) "Specification of Neurotransmitter Identity by *Phox2* Proteins in Neural Crest Stem Cells", *Neuron* 22:693-705 (Exhibit 31);
59. Lumsden, A. et al. (1996) "Patterning the Vertebrate Neuraxis", *Science* 274:1109-1115;
60. Markham, J.A. et al. (1991) "Migration Patterns of Sympathetic Preganglionic Neurons in Embryonic Rat Spinal Cord", *J. Neurobiol.* 22:811-822 (Exhibit 32);
61. Marti, E. et al. (1995) "Requirement of 19k Form of Sonic Hedgehog for Induction of Distinct Ventral Cell Types", *Nature* 375:322-325;
62. Matise M.P. et al. (1998) "Gli2 Is Required for Induction of Floor Plate and Adjacent Cells, but Not Most Ventral Neurons in the Mouse Central Nervous System", *Development*

125:2759-2770;

63. Matsuoka, T. et al. (1997) "Glycation-dependent, Reactive Oxygen Species-mediated Suppression of the Insulin Gene Promoter Activity in HIT Cells", *J. Clin. Invest.* 99:144-150 (**Exhibit 33**);
64. Naya, F.J. et al. (1997) "Diabetes, Defective Pancreatic Morphogenesis, and Abnormal Enteroendocrine Differentiation in BETA2/NeuroD-deficient Mice", *Genes & Dev.* 11:2323-2334 (**Exhibit 34**);
65. O'Brien, M.K. et al. (1990) "Development and Survival of Thoracic Motoneurons and Hindlimb Musculature Following Transplantation of the Thoracic Neural Tube to the Lumbar Region in the Chick Embryo: Anatomical Aspects", *J. Neurobiol.* 21:313-340 (**Exhibit 35**);
66. O'Brien, M.K. et al. (1990) "Development and Survival of Thoracic Motoneurons and Hindlimb Musculature Following Transplantation of the Thoracic Neural Tube to the Lumbar Region in the Chick Embryo: Functional Aspects", *J. Neurobiol.* 21:341-355 (**Exhibit 36**);
67. Offield, M.F. et al. (1996) "PDX-1 is Required for Pancreatic Outgrowth and Differentiation of the Rostral Duodenum", *Development* 122:983-995 (**Exhibit 37**);
68. Ohlsson, H. et al. (1993) "IPF1, a Homeodomain-containing Transactivator of the Insulin Gene", *EMBO J.* 12:4251-4259

(Exhibit 38);

69. Olson, L.K. et al. (1998) "Glucose Rapidly and Reversibly Decreases INS-1 Cell Insulin Gene Transcription via Decrements in STF-1 and C1 Activator Transcription Factor Activity", *Mol. Endocrinol.* 12:207-219 (Exhibit 39);
70. Osumi, N. et al. (1997) "Pax-6 Is Involved in Specification of the Hindbrain Motor Neuron Subtype", *Development* 124:2961-2972;
71. Pabst, O. et al. (1998) "Nkx2.9 Is a Novel Homeobox Transcription Factor Which Demarcates Ventral Domains in the Developing Mouse CNS", *Mech. Dev.* 73:85-93;
72. Pattyn, A. et al. (1997) "Expression and Interactions of the Two Closely Related Homeobox Genes Phox2a and Phox2b During Neurogenesis", *Development* 124: 4065-4075;
73. Pattyn, A. et al. (1999) "The Homeobox Gene *Phox2b* is Essential for the Development of Autonomic Neural Crest Derivatives", *Nature* 399:366-370 (Exhibit 40);
74. Pfaff, S. L. et al. (1996) "Requirement for LIM Homeobox Gene *Isl1* in Motor Neuron Generation Reveals a Motor Neuron-dependent Step in Interneuron Differentiation", *Cell* 84:309-320;
75. Pfaff, S. et al. (1998) "Neuronal Diversification: Development of Motor Neuron Subtypes", *Curr. Opin.*

Neurobiol. 8:27-36;

76. Pharmacia Biotech catalogue (1995) p. 277;
77. Pharmacia Biotech catalogue (1995) pp. 104-111;
78. Pictet, R., & Rutter, W.J. (1972) "Development of the Embryonic Endocrine Pancreas" in *HANDBOOK OF PHYSIOLOGY*, eds., D.F. Steiner, and N. Frenkel (Williams and Wilkins; Washinton, D.C.) pp. 25-66 (**Exhibit 41**);
79. Pignoni, F. et al. (1997) "The Eye-Specification Proteins So and Eya Form a Complex and Regulate Multiple Steps in Drosophila Eye Development", *Cell* 91:881-891;
80. Riddle, R.D. et al. (1995) "Induction of the LIM Homeobox Gene *Lmx1* by WNT7a Establishes Dorsoventral Pattern in the Vertebrate Limb", *Cell* 83:631-640;
81. Roelink, H. et al. (1995) "Floor Plate and Motor Neuron Induction by Different Concentrations of the Amino-Terminal Cleavage Product of Sonic Hedgehog Autoproteolysis", *Cell* 81:445-455;
82. Ross, A.J. et al. (1998) "A Homeobox Gene, *HLXB9*, is the Major Locus for Dominantly Inherited Sacral Agenesis", *Nat. Genet.* 20:358-361 (**Exhibit 42**);
83. Roztocil, T. et al. (1997) "NeuroM, a Neural Helix-loop-helix Transcription Factor, Defines a New Transition

Stage in Neurogenesis", *Development* 124:3263-3272;

84. Ruiz i Altaba et al. (1993) "Ectopic Neural Expression of a Floor Plate Marker in Frog Embryos Injected with the Midline Transcription Factor *Pintallavis*", *Proc. Natl. Acad. Sci. USA* 90:8268-8272;
85. Ruiz i Altaba et al. (1995) "Restrictions to Floor Plate Induction by Hedgehog and Winged-helix Genes in the Neural Tube of Frog Embryos", *Mol. Cell Neurosci.* 6:106-121;
86. Saha, M.S. et al. (1997) "Dorsal-Ventral Patterning During Neural Induction in *Xenopus*: Assessment of Spinal Cord Regionalization with *xHB9*, a Marker for the Motor Neuron Region", *Dev. Biol.* 187:209-223;
87. Sander M. et al. (1997) "Genetic Analysis Reveals that *PAX6* is Required for Normal Transcription of Pancreatic Hormone Genes and Islet Development", *Genes Dev.* 11:1662-1673 (**Exhibit 43**);
88. Sasaki, H. et al. (1994) "HNF-3 Beta as a Regulator of Floor Plate Development", *Cell* 76:103-115;
89. Schaeren-Wiemers, N. et al. (1993) "A Single Protocol to Detect Transcripts of Various Types and Expression Levels in Neural Tissue and Cultured Cells: in Situ Hybridization Using Digoxigenin-labeled cRNA Probes", *Histochemistry* 100:431-440;

90. Sharma, A. et al.. (1995) "The Reduction of Insulin Gene Transcription in HIT-T15 Beta Cells Chronically Exposed to High Glucose Concentration Is Associated with the Loss of RIPE3b1 and STF-1 Transcription Factor Expression", *Mol. Endocrinol.* 9:1127-1134 (**Exhibit 44**);
91. Sharma, K. et al. (1998) "LIM Homeodomain Factors Lhx3 and Lhx4 Assign Subtype Identities for Motor Neurons", *Cell* 95:817-828 (**Exhibit 45**);
92. Slack, J.M.W. (1995) "Developmental Biology of the Pancreas", *Development* 121:1569-1580 (**Exhibit 46**);
93. Sockanathan, S. et al. (1998) "Motor Neuron- Derived Retinoid Signaling Specifies the Subtype Identity of Spinal Motor Neurons", *Cell* 94:503-514 (**Exhibit 47**);
94. Sosa-Pineda, B. et al. (1997) "The Pax4 Gene Is Essential for Differentiation of Insulin-producing Beta Cells in the Mammalian Pancreas", *Nature* 386:399-402 (**Exhibit 48**);
95. Spooner, B.S. et al. (1970) "The Development of the Dorsal and Ventral Mammalian Pancreas In Vivo and In Vitro", *J. Cell Biol.* 47:235-246 (**Exhibit 49**);
96. Stoffers, D.A. et al. (1997) "Early-onset Type-II Diabetes Mellitus (MODY4) Linked to *IPF1*", *Nature Genet.* 17:138-139 (**Exhibit 50**);

97. Stoffers, D.A. et al. (1997) "Pancreatic Agenesis Attributable to a Single Nucleotide Deletion in the Human *IPF1* Gene Coding Sequence", *Nature Genet.* 15:106-110 (Exhibit 51);
98. St-Onge, L. et al. (1997) "*Pax6* Is Required for Differentiation of Glucagon-producing Alpha-cells in Mouse Pancreas", *Nature* 387:406-409 (Exhibit 52);
99. Sussel, L. et al. (1998) "Mice Lacking the Homeodomain Transcription Factor *Nkx2.2* Have Diabetes Due to Arrested Differentiation of Pancreatic Beta Cells", *Development* 125:2213-2221 (Exhibit 53);
100. Tanabe, Y. et al. (1995) "Induction of Motor Neurons by Sonic Hedgehog Is Independent of Floor Plate Differentiation", *Curr. Biol.* 5:651-658;
101. Tanabe, Y. et al. (1996) "Diversity and Pattern in the Developing Spinal Cord", *Science* 274:1115-1123;
102. Tanabe, Y. et al. (1998) "Specification of Motor Neuron Identity by the *MNR2* Homeodomain Protein", *Cell* 95:67-80;
103. Tanaka, H. et al. (1984) "Developmental Changes in Unique Cell Surface Antigens of Chick Embryo Spinal Motor Neurons and Ganglion Cells", *Dev. Biol.* 106:26-37;
104. Thaler et al. (1999) "Active Suppression of Interneuron Programs with Developing Motor Neurons Revealed by

Analysis of Homeodomain Factor HB9", *Neuron* 23:675-687;

105. Tosney, K.W. et al. (1985) "Development of the Major Pathways for Neurite Outgrowth in the Chick Hindlimb", *Dev. Biol.* 109:193-214 (**Exhibit 54**);
106. Tsuchida, T. (1994) "Topographic Organization of Embryonic Motor Neurons Defined by Expression of LIM Homeobox Genes", *Cell* 79:957-70;
107. Varela-Echavarría, A. et al. (1996) "Differential Expression of LIM Homeobox Genes among Motor Neuron Subpopulations in the Developing Chick Brain Stem", *Mol. Cell. Neurosci.* 8:242-257;
108. Weintraub, H. (1993) "The MyoD Family and Myogenesis: Redundancy, Networks, and Thresholds", *Cell* 75:1241-1244;
109. Wessells, N.K. & Cohen, J.H. (1967) "Early Pancreas Organogenesis: Morphogenesis, Tissue Interactions, and Mass Effects", *Dev. Biology* 15:237-270 (**Exhibit 55**);
110. Westendorf, J.M. et al. (1994) "Cloning of cDNAs for M-Phase Phosphoproteins Recognized by the MPM2 Monoclonal Antibody and Determination of the Phosphorylated Epitope", *Proc. Natl. Acad. Sci. USA* 91:714-718;
111. Wetts, R. et al. (1995) "Transient and Continuous Expression of NADPH Diaphorase in Different Neuronal Populations of Developing Rat Spinal Cord", *Dev. Dyn.*

Applicants: Thomas M. Jessell, et al.
U.S. Serial No: 09/820,598
Filed: March 29, 2001
Page 35

202:215-228 (**Exhibit 56**);

112. Wildling, R. et al. (1993) "Agenesis of the Dorsal Pancreas in a Woman with Diabetes Mellitus and in Both of Her Sons", *Gastroenterology* 104:1182-1186 (**Exhibit 57**);
113. Yamada, T. et al. (1993) "Control of Cell Pattern in the Neural Tube: Motor Neuron Induction of Diffusible Factors From Notochord and Floor Plate", *Cell* 73:673-686; and
114. Zhao, D. et al. (1996) "Molecular Identification of a Major Retinoic-Acid-Synthesizing Enzyme, a Retinaldehyde-Specific Dehydrogenase", *Eur. J. Biochem.* 240:15-22 (**Exhibit 58**).

The subject application is a continuation of PCT International Application No. PCT/US99/22517, filed September 29, 1999, designating the United States of America, which is a continuation-in-part of U.S. Serial No. 09/162,524, filed September 29, 1998, now U.S. Patent No. 6,387,656 B1, issued May 14, 2002, a copy of which patent is attached hereto as **Exhibit 1**.

Above listed references 8, 12, 14-15, 19, 21-22, 26, 31-32, 34-35, 38, 41-42, 44, 51-54, 57, 59, 61-62, 70-72, 74-75, 79-81, 83-86, 88-89, 100-103, 106-108, 110 and 113 were submitted to and considered by the United States Patent and Trademark Office in an Information Disclosure Statement filed on August 20, 1999 in connection with U.S. Serial No. 09/162,524, filed September 29, 1998, now U.S. Patent No. 6,387,656 B1, issued

Applicants: Thomas M. Jessell, et al.
U.S. Serial No: 09/820,598
Filed: March 29, 2001
Page 36

May 14, 2002. Above listed references 17, and 23-25 were cited by the United States Patent and Trademark Office in an Office Action dated October 22, 1999 in connection with U.S. Serial No. 09/162,524, filed September 29, 1998, now U.S. Patent No. 6,387,656 B1, issued May 14, 2002. Above listed reference 76 was cited by the United States Patent and Trademark Office in an Office Action dated July 20, 2000 in connection with U.S. Serial No. 09/162,524, filed September 29, 1998, now U.S. Patent No. 6,387,656 B1, issued May 14, 2002. Above listed reference 77 was cited by the United States Patent and Trademark Office in an Office Action dated April 11, 2001 in connection with U.S. Serial No. 09/162,524, filed September 29, 1998, now U.S. Patent No. 6,387,656 B1, issued May 14, 2002. Accordingly, under 37 C.F.R. §1.98(d) copies of these references are not required to be provided to the United States Patent and Trademark Office, since they were previously submitted to or cited by the United States Patent and Trademark Office in an application relied upon for an earlier filing date under 35 U.S.C. §120.

PCT International Application No. PCT/US99/22517, filed September 29, 1999, is a foreign counterpart application of the subject application. A copy of PCT International Application No. PCT/US99/22517 is attached hereto as **Exhibit 2**. A Search Report was issued on January 25, 2000 in connection with PCT International Application No. PCT/US99/22517, filed September 29, 1999. A copy of the Search Report is attached hereto as **Exhibit B**. Above listed references 11, 25, 39, 86 and 104 were cited in the Search Report. Above listed reference 86 was submitted to and

Applicants: Thomas M. Jessell, et al.
U.S. Serial No: 09/820,598
Filed: March 29, 2001
Page 37

considered by the United States Patent and Trademark Office in an Information Disclosure Statement filed on August 20, 1999 in connection with U.S. Serial No. 09/162,524, filed September 29, 1998. Above listed reference 25 was cited by the United States Patent and Trademark Office in an Office Action dated October 22, 1999 in connection with U.S. Serial No. 09/162,524, filed September 29, 1998. Above listed references 11 and 104 were submitted to and considered by the United States Patent and Trademark Office in a Supplemental Information Disclosure Statement filed on April 24, 2000 in connection with U.S. Serial No. 09/162,524, filed September 29, 1998. Above listed reference 39 was cited by the United States Patent and Trademark Office in an Office Action dated April 11, 2001 in connection with U.S. Serial No. 09/162,524, filed September 29, 1998. Accordingly, under 37 C.F.R. §1.98(d) copies of these references are not required to be provided to the United States Patent and Trademark Office, since they were previously submitted to or cited by the United States Patent and Trademark Office in an application relied upon for an earlier filing date under 35 U.S.C. §120.

U.S. Serial No. 10/095,932, filed March 11, 2002 is a divisional of U.S. Serial No. 09/162,524, filed September 29, 1998, now U.S. Patent No. 6,387,656 B1, issued May 14, 2002. A copy of U.S. Serial No. 10/095,932, including a Preliminary Amendment which applicants submitted to the U.S. Patent Office on March 11, 2002 which includes the currently pending claims, is attached hereto as **Exhibit 3**.

Applicants: Thomas M. Jessell, et al.
U.S. Serial No: 09/820,598
Filed: March 29, 2001
Page 38

Pursuant to 37 C.F.R. §1.97(c)(2), a \$180.00 fee is required in connection with the filing of this Information Disclosure Statement and a check which includes this amount is enclosed.

Summary

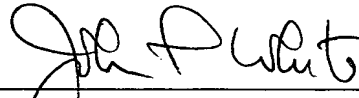
For the reasons set forth hereinabove, applicants respectfully request that the Examiner reconsider and withdraw the various grounds of rejection and objection and earnestly solicit allowance of the pending claims, i.e. claims 27, 45, 48, 49, 50, 52, 60 and 126-128.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

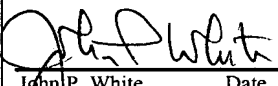
Applicants: Thomas M. Jessell, et al.
U.S. Serial No: 09/820,598
Filed: March 29, 2001
Page 39

No fee, other than the \$180.00 fee for submitting an Information Disclosure Statement under 37 C.F.R. §1.97(c)(2), is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



John P. White
Registration No. 28,678
Attorney for Applicant
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, New York 10036
(212) 278-0400

I hereby certify that this correspondence is being deposited this date with the U.S. postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.	
	5/11/04
John P. White	Date
Reg. No. 28,678	

Form PTO-1449

U.S. Department of Commerce
Patent and Trademark OfficeAtty. Docket No.
0575/57477-A-PCT-USSerial No.
09/820,598

INFORMATION DISCLOSURE CITATION

(Use several sheets if necessary)

Applicants:
Thomas M. Jessell et al.Filing Date
March 29, 2001Group
1653

U.S. PATENT DOCUMENTS

Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
	6 3 8 7 6 5 6	05/14/02	Jessell et al. (Exhibit 1)			

FOREIGN PATENT DOCUMENTS

Document Number	Date	Country	Class	Subclass	Translation
					Yes No
wo 0 0 1 8 8 8 4	04/06/00	PCT (Exhibit 2)			

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	U.S. Serial No. 10/095,932, filed March 11, 2002 on behalf of Thomas M. Jessell et al. (Exhibit 3);
	Ahlgren, U. et al. (1996) "The Morphogenesis of the Pancreatic Mesenchyme Is Uncoupled from That of the Pancreatic Epithelium in IPF1/PDX1-deficient Mice", <i>Development</i> 122:1409-1416 (Exhibit 4);
	Ahlgren, U. et al. (1997) "Independent Requirement for ISL1 in Formation of Pancreatic Mesenchyme and Islet Cells", <i>Nature</i> 385:257-260 (Exhibit 5);
	Ahlgren, U. et al. (1998) " β -Cell-Specific Inactivation of the Mouse <i>Ipfl/Pdx1</i> Gene Results in Loss Of the β -Cell Phenotype And Maturity Onset Diabetes", <i>Genes & Dev.</i> 12:1763-1768 (Exhibit 6);
	Aigner, L., et al. (1995) "Overexpression of the Neural Growth-Associated Protein GAP-43 Induces Nerve Sprouting in the Adult Nervous System of Transgenic Mice", <i>Cell</i> 83:269-278 (Exhibit 7);
	Anderson, D.J. et al. (1997) "The Determination of the Neuronal Phenotype" in <i>MOLECULAR AND CELLULAR APPROACHES TO NEURAL DEVELOPMENT</i> , eds. Cowan, W.M., Jessell, T.M., and Zipursky, S.L. (Oxford University Press; New York, Oxford), pp. 26-63;
	Apelqvist, Å., et al. (1997) "Sonic Hedgehog Directs Specialised Mesoderm Differentiation in the Intestine and Pancreas", <i>Current Biology</i> 7:801-804 (Exhibit 8);
	Appel, B., (1999) "LIMitless Combinations?", <i>Neuron</i> 22:3-5 (Exhibit 9);
	Arber et al. (1999) "Requirement for the Homeobox Gene <i>Hb9</i> in the Consolidation of Motor Neuron Identity", <i>Neuron</i> 23:659-674;
	Bang, A.G. et al. (1996) "Regulation of Vertebrate Neural Cell Fate by Transcription Factors", <i>Curr. Opin. Neurobiol.</i> 6:25-32;

EXAMINER

DATE CONSIDERED

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Applicant: Thomas M. Jessell et al.
U.S. Serial No.: 09/820,598
Filed: March 29, 2001
Exhibit A

Form PTO-1449

U.S. Department of Commerce
Patent and Trademark OfficeAtty. Docket No.
0575/57477-A-PCT-USSerial No.
09/820,598

INFORMATION DISCLOSURE CITATION

(Use several sheets if necessary)

Applicants:
Thomas M. Jessell et al.Filing Date
March 29, 2001Group
1653

U.S. PATENT DOCUMENTS

Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate

FOREIGN PATENT DOCUMENTS

Document Number	Date	Country	Class	Subclass	Translation	
					Yes	No

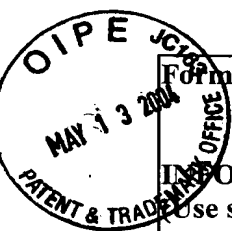
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Barber, R.P. et al. (1991) Generation Patterns of Immunocytochemically Identified Cholinergic Neurons at Autonomic Levels of the Rat Spinal Cord. <i>J. Comp. Neurol.</i> 311:509-519 (Exhibit 10);
	Basler, K. et al. (1993) "Control of Cell Pattern in the Neural Tube: Regulation of Cell Differentiation by Dorsalin-1, a Novel TGF Beta Family Member", <i>Cell</i> 73:687-702;
	Begley, C.G. et al. (1992) "Molecular Characterization of <i>nscl</i> , a Gene Encoding a Helix-loop-helix Protein Expressed in the Developing Nervous System", <i>Proc. Natl. Acad. Sci. USA</i> 89:38-42;
	Bitgood, M.J. et al. (1995) "Hedgehog and Bmp Genes Are Coexpressed at Many Diverse Sites of Cell-Cell Interaction in the Mouse Embryo", <i>Dev. Biol.</i> 172:126-138 (Exhibit 11);
	Branch, A.D. (1998) "A Good Antisense Molecule Is Hard To Find", <i>Trends in Biochemical Sciences</i> 23: 45-50;
	Briscoe, J. et al. (1999) "Homeobox Gene <i>Nkx2.2</i> and Specification of Neuronal Identity by Graded Sonic hedgehog Signalling", <i>Nature</i> 398:622-627 (Exhibit 12);
	Burke, A.C. et al. (1996) "Virally Mediated Misexpression of <i>Hoxc-6</i> in the Cervical Mesoderm Results in Spinal Nerve Truncations", <i>Dev. Biol.</i> 178:192-197;
	Cepko, C.L. (1999) "The Roles of Intrinsic and Extrinsic Cues and bHLH Genes in the Determination of Retinal Cell Fates", <i>Curr. Opin. Neurobiol</i> 9:37-46 (Exhibit 13);
	Chen, R. et al. (1997) "Dachshund and Eyes Absent Proteins Form a Complex and Function Synergistically to Induce Ectopic Eye Development in <i>Drosophila</i> ", <i>Cell</i> 91:893-903;

EXAMINER

DATE CONSIDERED

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.



Form PTO-1449

U.S. Department of Commerce
Patent and Trademark OfficeAtty. Docket No.
0575/57477-A-PCT-USSerial No.
09/820,598

INFORMATION DISCLOSURE CITATION

(Use several sheets if necessary)

Applicants:
Thomas M. Jessell et al.Filing Date
March 29, 2001Group
1653

U.S. PATENT DOCUMENTS

Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate

FOREIGN PATENT DOCUMENTS

Document Number	Date	Country	Class	Subclass	Translation
					Yes No

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Chiang, C. et al. (1996) "Cyclopia and Defective Axial Patterning in Mice Lacking Sonic Hedgehog Gene Function", <i>Nature</i> 383:407-413;
	Crook, ed. (1998) in <i>BASIC PRINCIPLES OF ANTISENSE THERAPEUTICS</i> (Springer-Verlag; New York), pp. 1 and 4;
	Database Tumor Gene Index (June 1998) Accession No. A1560820. NCI-CGAP. National Cancer Institute, Cancer Genome Anatomy Project (CGAP), Tumor Gene Index;
	Deguchi et al. (1991) "Nucleotide Sequence of a Novel Diverged Human Homeobox Gene Encodes a DNA Binding Protein", <i>Nucleic Acids Research</i> 19:3742;
	Ding, Q. et al. (1998) "Diminished Sonic Hedgehog Signaling and Lack of Floor Plate Differentiation in Gli2 Mutant Mice", <i>Development</i> 125:2533-2543;
	Dutta, S. et al. (1998) "Regulatory Factor Linked to Late-Onset Diabetes?", <i>Nature</i> 392:560 (Exhibit 14);
	Edlund, H. (1998) "Perspectives in Diabetes: Transcribing Pancreas", <i>Diabetes</i> 47:1817-1823 (Exhibit 15);
	Edlund, T. et al. (1999) "Progression from Extrinsic to Intrinsic Signaling in Cell Fate Specification: a View from the Nervous System", <i>Cell</i> 96:211-224 (Exhibit 16);
	Ensini, M. et al. (1998) "The Control of Rostrocaudal Pattern in the Developing Spinal Cord: Specification of Motor Neuron Subtype Identity Is Initiated by Signals from Paraxial Mesoderm", <i>Development</i> 125:969-982 (Exhibit 17);
	Ericson, J. et al. (1992) "Early Stages of Motor Neuron Differentiation Revealed by Expression of Homeobox Gene Islet-1", <i>Science</i> 256:1555-60;

EXAMINER

DATE CONSIDERED

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449

U.S. Department of Commerce
Patent and Trademark OfficeAtty. Docket No.
0575/57477-A-PCT-USSerial No.
09/820,598

INFORMATION DISCLOSURE CITATION

(Use several sheets if necessary)

Applicants:
Thomas M. Jessell et al.Filing Date
March 29, 2001Group
1653

U.S. PATENT DOCUMENTS

Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate

FOREIGN PATENT DOCUMENTS

Document Number	Date	Country	Class	Subclass	Translation
					Yes No

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Ericson, J. et al. (1996) "Two Critical Periods of Sonic Hedgehog Signaling Required for the Specification of Motor Neuron Identity", <i>Cell</i> 87:661-673;
	Ericson, J. et al. (1997) "Graded Sonic Hedgehog Signaling and the Specification of Cell Fate in the Ventral Neural Tube", <i>Cold Spring Harbor Symp. Quant. Biol.</i> 62:451-466 (Exhibit 18);
	Ericson, J. et al. (1997) "Pax6 Controls Progenitor Cell Identity and Neuronal Fate in Response to Graded Shh Signaling", <i>Cell</i> 90:169-180;
	Fedtsova, N. et al. (1997) "Inhibitory Effects of Ventral Signals on the Development of Brn-3.0-expressing Neurons in the Dorsal Spinal Cord", <i>Dev. Biol.</i> 190:18-31;
	Goridis, C. (1999) "Transcriptional Control of Neurotransmitter Phenotype", <i>Curr. Opin. Neurobiol.</i> 9:47-53 (Exhibit 19);
	Goulding, M. (1998) "Specifying Motor Neurons and Their Connections", <i>Neuron</i> 21:943-946 (Exhibit 20);
	Halder, G. et al. (1995) "Induction of Ectopic Eyes by Targeted Expression of the Eyeless Gene in <i>Drosophila</i> ", <i>Science</i> 267:1788-1792;
	Harrison, K.A. et al. (1994) "A Novel Human Homeobox Gene Distantly Related to Proboscipedia Is Expressed in Lymphoid and Pancreatic Tissues", <i>J. Biol. Chem.</i> 269:19968-19975;
	Hebrok, M. et al. (1998) "Notochord Repression of Endodermal Sonic Hedgehog Permits Pancreas Development", <i>Genes & Dev.</i> 12:1705-1713 (Exhibit 21);
	Hynes, M. et al. (1997) "Control of Cell Pattern in the Neural Tube by the Zinc Finger Transcription Factor and Oncogene Gli-1", <i>Neuron</i> 19:15-26;

EXAMINER

DATE CONSIDERED

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449

U.S. Department of Commerce
Patent and Trademark OfficeAtty. Docket No.
0575/57477-A-PCT-USSerial No.
09/820,598

INFORMATION DISCLOSURE CITATION

(Use several sheets if necessary)

Applicants:
Thomas M. Jessell et al.Filing Date
March 29, 2001Group
1653

U.S. PATENT DOCUMENTS

Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate

FOREIGN PATENT DOCUMENTS

Document Number	Date	Country	Class	Subclass	Translation	
					Yes	No

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Ingham, P.W. (1995) "Signaling by Hedgehog Family Proteins in <i>Drosophila</i> and Vertebrate Development", <i>Curr. Opin. Genet. Dev.</i> 5:492-498;
	Jonsson, J. et al. (1994) "Insulin-Promoter-Factor 1 is Required for Pancreas Development in Mice", <i>Nature</i> 371:606-609 (Exhibit 22);
	Jurata, L.W. et al. (1998) "The Nuclear LIM Domain Interactor Nli Mediates Homo- and Heterodimerization of Lim Domain Transcription Factors", <i>J. Biol. Chem.</i> 273:3152-3157;
	Kalter, H. (1993) "Case Reports of Malformations Associated with Maternal Diabetes: History and Critique", <i>Clin. Genet.</i> 43:174-179 (Exhibit 23);
	Kim, S.K. et al. (1997) "Notochord to Endoderm Signaling is Required for Pancreas Development", <i>Development</i> 124:4243-4252 (Exhibit 24);
	Krapp, A. et al. (1998) "The bHLH Protein PTF1-p48 is Essential for the Formation of the Exocrine and the Correct Spatial Organization of the Endocrine Pancreas", <i>Genes & Dev.</i> 12:3752-3763 (Exhibit 25);
	Lance-Jones, C. et al. (1981) "Pathway Selection by Embryonic Chick Motoneurons in an Experimentally Altered Environment", <i>Proceedings of the Royal Society of London, Series B, Biological Sciences</i> 214:19-52 (Exhibit 26);
	Landmesser, L. (1978a) "The Distribution of Motoneurons Supplying Chick Hind Limb Muscles", <i>J. Physiol.</i> 284:371-389 (Exhibit 27);
	Landmesser, L. (1978b) "The Development of Motor Projection Patterns in the Chick Hind Limb", <i>J. Physiol.</i> 284:391-414 (Exhibit 28);
	Langman, J. et al. (1966) "Behavior of Neuroepithelial Cells During Closure of the Neural Tube", <i>J. Comp. Neurol.</i> 127:399-411;

EXAMINER

DATE CONSIDERED

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance

Form PTO-1449	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No. 0575/57477-A-PCT-US	Serial No. 09/820,598
INFORMATION DISCLOSURE CITATION (Use several sheets if necessary)		Applicants: Thomas M. Jessell et al.	
		Filing Date March 29, 2001	Group 1653

U.S. PATENT DOCUMENTS

Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate

FOREIGN PATENT DOCUMENTS

Document Number	Date	Country	Class	Subclass	Translation	
					Yes	No

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Leber, S.M. et al. (1995) "Migratory Paths of Neurons and Glia in the Embryonic Chick Spinal Cord", <i>J. Neurosci.</i> 15:1236-1248; Lee, J. et al. (1997) "Gli1 Is a Target of Sonic Hedgehog That Induces Ventral Neural Tube Development", <i>Development</i> 124:2537-2552;
	Liem, K.F. et al. (1997) "A Role for the Roof Plate and its Resident TGF-beta-related Proteins in Neuronal Patterning in the Dorsal Spinal Cord", <i>Cell</i> 91:127-138; Lin, J.H. et al. (1998) "Functionally Related Motor Neuron Pool and Muscle Sensory Afferent Subtypes Defined by Coordinate <i>ETS</i> Gene Expression", <i>Cell</i> 95:393-407 (Exhibit 29);
	Liu, I.S.C. et al. (1994) "Developmental Expression of a Novel Murine Homeobox Gene (<i>Chx10</i>): Evidence for Roles in Determination of the Neuroretina and Inner Nuclear Layer", <i>Neuron</i> 13:377-393 (Exhibit 30); Lo, L. et al. (1998) "MASH1 Activates Expression of the Paired Homeodomain Transcription Factor <i>Phox2a</i> , and Couples Pan-neuronal and Subtype-specific Components of Autonomic Neuronal Identity", <i>Development</i> 125:609-620;
	Lo, L. et al. (1999) "Specification of Neurotransmitter Identity by <i>Phox2</i> Proteins in Neural Crest Stem Cells", <i>Neuron</i> 22:693-705 (Exhibit 31); Lumsden, A. et al. (1996) "Patterning the Vertebrate Neuraxis", <i>Science</i> 274:1109-1115;
	Markham, J.A. et al. (1991) "Migration Patterns of Sympathetic Preganglionic Neurons in Embryonic Rat Spinal Cord", <i>J. Neurobiol.</i> 22:811-822 (Exhibit 32); Marti, E. et al. (1995) "Requirement of 19k Form of Sonic Hedgehog for Induction of Distinct Ventral Cell Types", <i>Nature</i> 375:322-325;

EXAMINER	DATE CONSIDERED
----------	-----------------

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449

U.S. Department of Commerce
Patent and Trademark OfficeAtty. Docket No.
0575/57477-A-PCT-USSerial No.
09/820,598

INFORMATION DISCLOSURE CITATION

(Use several sheets if necessary)

Applicants:
Thomas M. Jessell et al.Filing Date
March 29, 2001Group
1653

U.S. PATENT DOCUMENTS

Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate

FOREIGN PATENT DOCUMENTS

Document Number	Date	Country	Class	Subclass	Translation	
					Yes	No

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Matise M.P. et al. (1998) "Gli2 Is Required for Induction of Floor Plate and Adjacent Cells, but Not Most Ventral Neurons in the Mouse Central Nervous System", <i>Development</i> 125:2759-2770; Matsuka, T. et al. (1997) "Glycation-dependent, Reactive Oxygen Species-mediated Suppression of the Insulin Gene Promoter Activity in HIT Cells", <i>J. Clin. Invest.</i> 99:144-150 (Exhibit 33);
	Naya, F.J. et al. (1997) "Diabetes, Defective Pancreatic Morphogenesis, and Abnormal Enteroendocrine Differentiation in BETA2/NeuroD-deficient Mice", <i>Genes & Dev.</i> 11:2323-2334 (Exhibit 34); O'Brien, M.K. et al. (1990) "Development and Survival of Thoracic Motoneurons and Hindlimb Musculature Following Transplantation of the Thoracic Neural Tube to the Lumbar Region in the Chick Embryo: Anatomical Aspects", <i>J. Neurobiol.</i> 21:313-340 (Exhibit 35);
	O'Brien, M.K. et al. (1990) "Development and Survival of Thoracic Motoneurons and Hindlimb Musculature Following Transplantation of the Thoracic Neural Tube to the Lumbar Region in the Chick Embryo: Functional Aspects", <i>J. Neurobiol.</i> 21:341-355 (Exhibit 36); Offield, M.F. et al. (1996) "PDX-1 is Required for Pancreatic Outgrowth and Differentiation of the Rostral Duodenum", <i>Development</i> 122:983-995 (Exhibit 37);
	Ohlsson, H. et al. (1993) "IPF1, a Homeodomain-containing Transactivator of the Insulin Gene", <i>EMBO J.</i> 12:4251-4259 (Exhibit 38); Olson, L.K. et al. (1998) "Glucose Rapidly and Reversibly Decreases INS-1 Cell Insulin Gene Transcription via Decrements in STF-1 and C1 Activator Transcription Factor Activity", <i>Mol. Endocrinol.</i> 12:207-219 (Exhibit 39);

EXAMINER

DATE CONSIDERED

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449

U.S. Department of Commerce
Patent and Trademark OfficeAtty. Docket No.
0575/57477-A-PCT-USSerial No.
09/820,598

INFORMATION DISCLOSURE CITATION

(Use several sheets if necessary)

Applicants:
Thomas M. Jessell et al.Filing Date
March 29, 2001Group
1653

U.S. PATENT DOCUMENTS

Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate

FOREIGN PATENT DOCUMENTS

Document Number	Date	Country	Class	Subclass	Translation	
					Yes	No

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Osumi, N. et al. (1997) "Pax-6 Is Involved in Specification of the Hindbrain Motor Neuron Subtype", <i>Development</i> 124:2961-2972;
	Pabst, O. et al. (1998) "Nkx2.9 Is a Novel Homeobox Transcription Factor Which Demarcates Ventral Domains in the Developing Mouse CNS", <i>Mech. Dev.</i> 73:85-93;
	Pattyn, A. et al. (1997) "Expression and Interactions of the Two Closely Related Homeobox Genes Phox2a and Phox2b During Neurogenesis", <i>Development</i> 124: 4065-4075;
	Pattyn, A. et al. (1999) "The Homeobox Gene Phox2b is Essential for the Development of Autonomic Neural Crest Derivatives", <i>Nature</i> 399:366-370 (Exhibit 40);
	Pfaff, S. L. et al. (1996) "Requirement for LIM Homeobox Gene Isl1 in Motor Neuron Generation Reveals a Motor Neuron-dependent Step in Interneuron Differentiation", <i>Cell</i> 84:309-320;
	Pfaff, S. et al. (1998) "Neuronal Diversification: Development of Motor Neuron Subtypes", <i>Curr. Opin. Neurobiol.</i> 8:27-36;
	Pharmacia Biotech catalogue (1995) p. 277;
	Pharmacia Biotech catalogue (1995) pp. 104-111;
	Pictet, R., & Rutter, W.J. (1972) "Development of the Embryonic Endocrine Pancreas" in <i>HANDBOOK OF PHYSIOLOGY</i> , eds., D.F. Steiner, and N. Frenkel (Williams and Wilkins; Washinton, D.C.) pp. 25-66 (Exhibit 41);
	Pignoni, F. et al. (1997) "The Eye-Specification Proteins So and Eya Form a Complex and Regulate Multiple Steps in Drosophila Eye Development", <i>Cell</i> 91:881-891;
	Riddle, R.D. et al. (1995) "Induction of the LIM Homeobox Gene <i>Lmx1</i> by WNT7a Establishes Dorsoventral Pattern in the Vertebrate Limb", <i>Cell</i> 83:631-640;
	Roelink, H. et al. (1995) "Floor Plate and Motor Neuron Induction by Different Concentrations of the Amino-Terminal Cleavage Product of Sonic Hedgehog Autoproteolysis", <i>Cell</i> 81:445-455;

EXAMINER

DATE CONSIDERED

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449

U.S. Department of Commerce
Patent and Trademark OfficeAtty. Docket No.
0575/57477-A-PCT-USSerial No.
09/820,598

INFORMATION DISCLOSURE CITATION

(Use several sheets if necessary)

Applicants:
Thomas M. Jessell et al.Filing Date
March 29, 2001Group
1653

U.S. PATENT DOCUMENTS

Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate

FOREIGN PATENT DOCUMENTS

Document Number	Date	Country	Class	Subclass	Translation	
					Yes	No

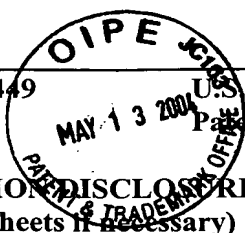
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Ross, A.J. et al. (1998) "A Homeobox Gene, <i>HLXB9</i> , is the Major Locus for Dominantly Inherited Sacral Agenesis", <i>Nat. Genet.</i> 20:358-361 (Exhibit 42);
	Roztocil, T. et al. (1997) "NeuroM, a Neural Helix-loop-helix Transcription Factor, Defines a New Transition Stage in Neurogenesis", <i>Development</i> 124:3263-3272;
	Ruiz i Altaba et al. (1993) "Ectopic Neural Expression of a Floor Plate Marker in Frog Embryos Injected with the Midline Transcription Factor <i>Pintallavis</i> ", <i>Proc. Natl. Acad. Sci. USA</i> 90:8268-8272;
	Ruiz i Altaba et al. (1995) "Restrictions to Floor Plate Induction by Hedgehog and Winged-helix Genes in the Neural Tube of Frog Embryos", <i>Mol. Cell Neurosci.</i> 6:106-121;
	Saha, M.S. et al. (1997) "Dorsal-Ventral Patterning During Neural Induction in Xenopus: Assessment of Spinal Cord Regionalization with <i>xHB9</i> , a Marker for the Motor Neuron Region", <i>Dev. Biol.</i> 187:209-223;
	Sander M. et al. (1997) "Genetic Analysis Reveals that <i>PAX6</i> is Required for Normal Transcription of Pancreatic Hormone Genes and Islet Development", <i>Genes Dev.</i> 11:1662-1673 (Exhibit 43);
	Sasaki, H. et al. (1994) "HNF-3 Beta as a Regulator of Floor Plate Development", <i>Cell</i> 76:103-115;
	Schaeren-Wiemers, N. et al. (1993) "A Single Protocol to Detect Transcripts of Various Types and Expression Levels in Neural Tissue and Cultured Cells: in Situ Hybridization Using Digoxigenin-labeled cRNA Probes", <i>Histochemistry</i> 100:431-440;
	Sharma, A. et al. (1995) "The Reduction of Insulin Gene Transcription in HIT-T15 Beta Cells Chronically Exposed to High Glucose Concentration Is Associated with the Loss of <i>RIPE3b1</i> and <i>STF-1</i> Transcription Factor Expression", <i>Mol. Endocrinol.</i> 9:1127-1134 (Exhibit 44);

EXAMINER

DATE CONSIDERED

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449		U.S. Department of Commerce Patent and Trademark Office		Atty. Docket No. 0575/57477-A-PCT-US		Serial No. 09/820,598	
 INFORMATION DISCLOSURE CITATION (Use several sheets if necessary)				Applicants: Thomas M. Jessell et al.			
				Filing Date March 29, 2001		Group 1653	
U.S. PATENT DOCUMENTS							
Examiner Initial		Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
FOREIGN PATENT DOCUMENTS							
		Document Number	Date	Country	Class	Subclass	Translation
							Yes No
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)							
		Sharma, K. et al. (1998) "LIM Homeodomain Factors Lhx3 and Lhx4 Assign Subtype Identities for Motor Neurons", <i>Cell</i> 95:817-828 (Exhibit 45);					
		Slack, J.M.W. (1995) "Developmental Biology of the Pancreas", <i>Development</i> 121:1569-1580 (Exhibit 46);					
		Sockanathan, S. et al. (1998) "Motor Neuron- Derived Retinoid Signaling Specifies the Subtype Identity of Spinal Motor Neurons", <i>Cell</i> 94:503-514 (Exhibit 47);					
		Sosa-Pineda, B. et al. (1997) "The Pax4 Gene Is Essential for Differentiation of Insulin-producing Beta Cells in the Mammalian Pancreas", <i>Nature</i> 386:399-402 (Exhibit 48);					
		Spooner, B.S. et al. (1970) "The Development of the Dorsal and Ventral Mammalian Pancreas In Vivo and In Vitro", <i>J. Cell Biol.</i> 47:235-246 (Exhibit 49);					
		Stoffers, D.A. et al. (1997) "Early-onset Type-II Diabetes Mellitus (MODY4) Linked to <i>IPF1</i> ", <i>Nature Genet.</i> 17:138-139 (Exhibit 50);					
		Stoffers, D.A. et al. (1997) "Pancreatic Agenesis Attributable to a Single Nucleotide Deletion in the Human <i>IPF1</i> Gene Coding Sequence", <i>Nature Genet.</i> 15:106-110 (Exhibit 51);					
		St-Onge, L. et al. (1997) "Pax6 Is Required for Differentiation of Glucagon-producing Alpha-cells in Mouse Pancreas", <i>Nature</i> 387:406-409 (Exhibit 52);					
		Sussel, L. et al. (1998) "Mice Lacking the Homeodomain Transcription Factor Nkx2.2 Have Diabetes Due to Arrested Differentiation of Pancreatic Beta Cells", <i>Development</i> 125:2213-2221 (Exhibit 53);					
		Tanabe, Y. et al. (1995) "Induction of Motor Neurons by Sonic Hedgehog Is Independent of Floor Plate Differentiation", <i>Curr. Biol.</i> 5:651-658;					
EXAMINER			DATE CONSIDERED				

***EXAMINER:** Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449		U.S. Department of Commerce Patent and Trademark Office		Atty. Docket No. 0575/57477-A-PCT-US	Serial No. 09/820,598		
INFORMATION DISCLOSURE CITATION (Use several sheets if necessary)				Applicants: Thomas M. Jessell et al.			
				Filing Date March 29, 2001	Group 1653		
U.S. PATENT DOCUMENTS							
Examiner Initial		Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
FOREIGN PATENT DOCUMENTS							
		Document Number	Date	Country	Class	Subclass	Translation
							Yes No
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)							
		Tanabe, Y. et al. (1996) "Diversity and Pattern in the Developing Spinal Cord", <i>Science</i> 274:1115-1123;					
		Tanabe, Y. et al. (1998) "Specification of Motor Neuron Identity by the MNR2 Homeodomain Protein", <i>Cell</i> 95:67-80;					
		Tanaka, H. et al. (1984) "Developmental Changes in Unique Cell Surface Antigens of Chick Embryo Spinal Motor Neurons and Ganglion Cells", <i>Dev. Biol.</i> 106:26-37;					
		Thaler et al. (1999) "Active Suppression of Interneuron Programs with Developing Motor Neurons Revealed by Analysis of Homeodomain Factor HB9", <i>Neuron</i> 23:675-687;					
		Tosney, K.W. et al. (1985) "Development of the Major Pathways for Neurite Outgrowth in the Chick Hindlimb", <i>Dev. Biol.</i> 109:193-214 (Exhibit 54);					
		Tsuchida, T. (1994) "Topographic Organization of Embryonic Motor Neurons Defined by Expression of LIM Homeobox Genes", <i>Cell</i> 79:957-70;					
		Varela-Echavarría, A. et al. (1996) "Differential Expression of LIM Homeobox Genes among Motor Neuron Subpopulations in the Developing Chick Brain Stem", <i>Mol. Cell. Neurosci.</i> 8:242-257;					
		Weintraub, H. (1993) "The MyoD Family and Myogenesis: Redundancy, Networks, and Thresholds", <i>Cell</i> 75:1241-1244;					
		Wessells, N.K. & Cohen, J.H. (1967) "Early Pancreas Organogenesis: Morphogenesis, Tissue Interactions, and Mass Effects", <i>Dev. Biology</i> 15:237-270 (Exhibit 55);					
		Westendorf, J.M. et al. (1994) "Cloning of cDNAs for M-Phase Phosphoproteins Recognized by the MPM2 Monoclonal Antibody and Determination of the Phosphorylated Epitope", <i>Proc. Natl. Acad. Sci. USA</i> 91:714-718;					
		Wetts, R. et al. (1995) "Transient and Continuous Expression of NADPH Diaphorase in Different Neuronal Populations of Developing Rat Spinal Cord", <i>Dev. Dyn.</i> 202:215-228 (Exhibit 56);					
EXAMINER			DATE CONSIDERED				
*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.							

Form PTO-1449

U.S. Department of Commerce
Patent and Trademark OfficeAtty. Docket No.
0575/57477-A-PCT-USSerial No.
09/820,598

INFORMATION DISCLOSURE CITATION

(Use several sheets if necessary)

Applicants:
Thomas M. Jessell et al.Filing Date
March 29, 2001Group
1653

U.S. PATENT DOCUMENTS

Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate

FOREIGN PATENT DOCUMENTS

Document Number	Date	Country	Class	Subclass	Translation	
					Yes	No

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Wildling, R. et al. (1993) "Agenesis of the Dorsal Pancreas in a Woman with Diabetes Mellitus and in Both of Her Sons", <i>Gastroenterology</i> 104:1182-1186 (Exhibit 57);
	Yamada, T. et al. (1993) "Control of Cell Pattern in the Neural Tube: Motor Neuron Induction of Diffusible Factors From Notochord and Floor Plate", <i>Cell</i> 73:673-686; and
	Zhao, D. et al. (1996) "Molecular Identification of a Major Retinoic-Acid-Synthesizing Enzyme, a Retinaldehyde-Specific Dehydrogenase", <i>Eur. J. Biochem.</i> 240:15-22 (Exhibit 58).

EXAMINER

DATE CONSIDERED

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.